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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,292	01/02/2004	Mark A. Hoffman	CRNC.107055	1596

46169 7590 02/27/2007

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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/751,292	HOFFMAN ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of record has changed. Please direct all further correspondence to Karlheinz R. Skowronek whose telephone number is (571) 272-9047.

Claim status

Claims 1-31 are canceled.

Claims 31-52 are new and being examined.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4 December 2006 has been entered.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37,38, 40,46, 47 and 51-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "common" in claim 40 is a relative term which renders the claim indefinite. The term "common" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the

art would not be reasonably apprised of the scope of the invention. It is unclear what Common means in the context of the claim. Does common mean that the first and second databases are the same database? Alternatively does the term common refer to the databases being well known?

The term "atypical event" in claim 37, 38, 46, 47, 51 and 52 is a relative term which renders the claim indefinite. The term "atypical event" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification uses the language "includes" but do provide a limit making the term indefinite. What is atypical or conversely what is would constitute a typical events?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-52 rejected under 35 U.S.C. 102(b) as being anticipated by Kobrinskii et al (Biomedical Engineering, Vol. 31, No. 3, p. 172-174), as evidenced by Steadman's Medical Dictionary (entries for heredity and inheritance, 2000).

The claims are directed to a method (claims 32-40 and 49-52) and system (claims 41-48) of determining the probability that the a person has a gene mutation by receiving a request for genetic test results for a patient; querying a database for the results; if the genetic test results do not exist, obtain the route of inheritance for the gene; query a database to identify any family members with genetic test results with the route of inheritance; use the genetic results of the identified family members to calculate the probability that the patient has a gene mutation; report the probability that the patient has a gene mutation.

Kobrinskii et al teach a system/method with the limitations of the instant claims. The system of Kobrinskii et al makes use of a national healthcare database (cl. 33, 42, 40) to provide the likelihood of gene mutations in individuals. Queries of the first and second database to obtain information regarding the individual and the individuals family to present a calculated likelihood the individual has a gene mutation (p. 172, para. 7-8) or has a mutation that could indicative of genotoxic environmental factors (interpreted as atypical events) (p. 172, para 2) (cl. 37, 38, 46, 47, 51, and 52) are taught by Kobrinskii et al. The teaching control of dispensary observations by Kobrinskii et al also reads on the limitation of cl. 48 of queries occurring in response to an order for medication (p. 172, para 2). Kobrinskii et al teach the system also contains an algorithm for compiling medical conclusions that are based on analysis of the database information including pedigree/genealogical tree (p. 172, para. 6) reading on claims 32, 34, 35, 41, 43, 44, and 49. The method instructions are embodied in at least 1 computer readable media, reading on claims 36 and 50 (p. 172, para 3). Kobrinskii et al teach the

calculation of the type of heredity (p. 172, para 7) prognosis of the risk of inherited diseases in a given family reading on claim 39 and 48, modes of inheritance (p. 172, para 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pathak et al (Proceedings of the Tenth Conference on Artificial Intelligence for Applications, p. 164- 170, March 1994).

The claims are directed to a method (claims 32-40 and 49-52) and system (claims 41-48) of determining the probability that the a person has a gene mutation by receiving a request for genetic test results for a patient; querying a database for the results; if the genetic test results do not exist, obtain the route of inheritance for the gene; query a database to identify any family members with genetic test results with the route of inheritance; use the genetic results of the identified family members to calculate the probability that the patient has a gene mutation; report the probability that the patient has a gene mutation.

Pathak et al teach a computerized method and system for automatically reporting genetic risk, i.e. the probability of a gene mutation. The method of Pathak et al relies on

case data for a patient. The system analyzes the data and produces a probability of the presence of a mutation. The input of case data as depicted in fig. 1 conceptually demonstrates data that is stored and utilized by the system, thereby reading on the limitation of a database. Consistent with the limitation of a database is the blackboard (p.165, col. 2, para. 1), a global data structure. Pathak et al teach the input as a set of objects each having the attributes name, sex, parents, siblings, spouse, children, loci (p.165, col. 2, para. 1). The attribute *loci*, as Pathak et al teach, is a set of alleles in the genome reading on the limitation of genetic test results (p.165, col. 2, para. 1). Pathak et al teach the use of rule sets to define queries of the case data to identify the route of inheritance based on familial relationships as well as to utilize the loci information to calculate a probability of an allele's presence (p.165, col. 2, para. 2 and p. 166, col. 2, #8).

It would have been obvious to apply the method/system of Pathak et al to practice the instant invention because a clinician would want to know what the probability is that a mutation is linked or correlated with an event that is not typical for the condition and because the method/system of Pathak et al is modular (p. 169, col 2, para 1). Further it would be obvious for a clinician to inquire the risk associated with having a gene form which would result in an adverse reaction to a prescribed treatment. This is a well known function that every clinician performs each time a treatment for a condition is prescribed. As with every treatment, a clinician first determines if the condition exists in a patient through examination, diagnostic tests in order to prescribe potential modes of treatment, then consults (queries) the family history for previous

instances of the condition under a defined genetic background. After considering the family history, the clinician then determines given the genetic background of the patient which prescribed mode of treatment yields the lowest risk of adverse reaction. The limitation of querying the patient record/database and the family history record/database upon prescription of medication merely automates a well known process of the medical arts and is therefore obvious.

One would have been motivated to do so because Pathak et al teach the method/system allows the study of any given case with any number of observations and assumptions (p. 169, col 1, para 1), the system streamlines the computation of risk which are used to make critical medical decisions (p. 169, col 2, para 2) and method/system automates error-prone, complex, tedious process to be a valuable aid to clinicians(p. 164, col.1, para. 1).

Regarding claims 34 and 43, Pathak et al teach knowledge source 2 concerned with allele inheritance relations with in the pedigree (p. 165, col. 2, "allele flow").

Regarding claims 35 and 44, Pathak et al teach calculating a likelihood the individual has a mutated form of the gene using the genetic markers (alleles) of at least one family member (p. 166, col. 2, "possible–explanations" and "Bayesian-analysis").

Regarding claim 36, Pathak et al teach a computer readable media comprising the instructions for the method (p. 169, col. 2, para 2, "software").

Regarding claims 37 and 46, the determination of gene variant that is indicative of atypical event is taught by Pathak et al in light of the statement that genetic risk is computed by considering disease characteristics (p. 164, col 1, para 1, lines 4-6).

Response to treatment or therapy is view to be an example of a disease characteristic, For example, the response or lack of response of breast cancer to taxol treatment is a characteristic of the disease. The application of rule 6 (p. 166, col. 2) to the data would result in the determination of previous atypical event that had occurred in any members of the family because rule 6 is directed to determining observable events. Since an atypical event is observable, rule 6 can be used to determine if a genetic variant is indicative of an atypical event.

Regarding claims 38 and 47, presenting an alert to a user, if the gene variant is indicative of an atypical event, Pathak et al teach rule 9 (p. 167, col. 1, "system-output"). The teaching of rule 9 reads on presenting an alert to the user since the output can be modulated by the user, for example to provide explanations for probabilities that exceed a threshold value

Regarding claim 39 and 48, Pathak et al teach the example of x-linked mode of inheritance (p. 167, col. 1, "X-linked").

Regarding claims 33, 40, 42 and 45, as addressed for claim 40 above in the rejection under 35 USC112, 2nd Paragraph, the use of the term "common" is unclear. For the purpose of this rejection the term "common" is being interpreted to mean to indicate that the first and second databases are a single record for the individual from a single database. Pathak et al teach that all a user must do is provide the system with the relevant data (p. 169, col 1., last three lines). It is common for an individual's medical information to exist in electronic form and comprise medical data of related family members. Therefore the teaching of providing the system with the relevant data

is viewed to read on the limitations of electronic records from a comprehensive healthcare database.

Regarding claims 49-52, the limitations are taught in part as above.

Claims 32-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coulson et al (Methods of Information in Medicine 2001; 40; 315-322.).

The claims are directed to a method (claims 32-40 and 49-52) and system (claims 41-48) of determining the probability that the a person has a gene mutation by receiving a request for genetic test results for a patient; querying a database for the results; if the genetic test results do not exist, obtain the route of inheritance for the gene; query a database to identify any family members with genetic test results with the route of inheritance; use the genetic results of the identified family members to calculate the probability that the patient has a gene mutation; report the probability that the patient has a gene mutation.

Coulson et al teach a method and system to determine and present the likelihood that a person has a genetic mutation (section 2, para 1 lines 7-10). Through the query of family member genetic data the method and system of Coulson et al identify a family member within the mode of inheritance. Coulson et al teach in figure 4 that for every route of inheritance, a likelihood ("risk score") is determined, reading on the steps of obtaining the mode inheritance, querying the family database and utilizing family member information to calculate likelihood. Coulson et al teach patient and family

database in a system that stores information about family members (section 2.1 para 1, line 4).

It would have been obvious to use the method of Coulson et al to practice the instant invention because clinicians would inquire the risk associated with having a gene form which would result in an adverse reaction to a prescribed treatment. This is a well known function that every clinician performs each time a treatment for a condition is prescribed. As with every treatment, a clinician first determines if the condition exists in a patient through examination, diagnostic tests in order to prescribe potential modes of treatment, then consults (queries) the family history for previous instances of the condition under a defined genetic background. After considering the family history, the clinician then determines given the genetic background of the patient which prescribed mode of treatment yields the lowest risk of adverse reaction. The limitation of querying the patient record/database and the family history record/database upon prescription of medication merely automates a well known process of the medical arts and is therefore obvious.

One would have been motivated to do so because Coulson et al teach the system saves time, reduces the confusion produced by a multitude of guidelines for risk assessment, and simplifies the assessment process (sect 1 para. 4).

Regarding claims 33, 40, 42 and 45, as addressed for claim 40 above in the rejection under 35 USC112, 2nd Paragraph, the use of the term "common" is unclear. For the purpose of this rejection the term "common" is being interpreted to mean to indicate that the first and second databases are a single record for the individual from a

single database. Coulson et al teach taking a patients family history (section 1, para. 3, lines 5-6) and storing it in the system (section 2.1 para 1, line 4). Although Coulson et al do not specifically address consulting a comprehensive database to find data, it would be obvious for a clinician to consult a comprehensive healthcare database to determine if the family and patient data had been previously entered to electronically access both the patient and family information rather duplicating the tedious work of manually entering the information into the system. It is well known that a patient's medical information exist in electronic form and comprise medical data of related family members (cf. Kobrinskii et al).

Regarding claims 34 and 43, the inquiry if a family member has a marker in the mode of inheritance, Coulson et al teach the color-coding of a pedigree to indicate the presence and type of genetic disorder in the members (sect 2.12, line 2-3). It is obvious this would also make the mode of inheritance apparent.

Regarding claims 35 and 44, Coulson et al teach calculating a likelihood the individual has a mutated form of the gene using the genetic markers (alleles) of at least one family member (figure 4).

Regarding claim 36, Coulson et al teach the instructions for the method are embodied on one or more computer readable medium as the article with the description of the system and how it works are on the Coulson et al website as well as the publishers website and are publicly available.

Regarding claim 37 and 46, determine if the gene mutation is indicative of a atypical event, Coulson et al teach the system provides recommendations for patient

management (section 2, para 1 lines 7-10). One of ordinary skill in the art will appreciate that "patient management" includes the identification of specific healthcare needs and the formulation of an effective treatment plan.

Regarding claim 38 and 47, directed to alerting the user to the presence of a mutation indicative of an atypical event, Coulson et al teach the system makes recommendation and provides an explanation of the results (section 2, para 1 lines 7-10). This is viewed as reading on alerting the user.

Regarding claim 39 and 48, the mode of inheritance, as addressed above the system of Coulson et al determines all modes of inheritance for a disease through a pedigree reading on the X-linked, Y-linked, Mendelian, and mitochondrial routes of inheritance.

Regarding claims 49-52, the limitations are taught in part as above.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karlheinz R. Skowronek/

MICHAEL BORIN, PH.D
PRIMARY EXAMINER